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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/000,113	10/30/2001	Grant L. Schoenhard	PAIN-003/03US	8969

23446 7590 07/26/2004

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EXAMINER	
KIM, VICKIE Y	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/000,113	SCHOENHARD, GRANT L.	
	Examiner	Art Unit	
	Vickie Kim	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-393* is/are pending in the application.

4a) Of the above claim(s) *1-361,370-372 and 377-393* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *362-369 and 373-376* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Acknowledgement is made of amendment filed April 22, 2004. Upon entering the amendment, the claims 362, 364,373 and 375 are amended.

2. The claims 362-369 and 373-376 are pending and presented for the examination.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 362-369, 373-374, 376 are rejected under 35 U.S.C. 102(e) as being anticipated by Craine(US2003/0148941 A1).

The claims are drawn to a composition comprising (a) non-opioid CNS-active agent; and (b) an opioid receptor antagonist in an amount in the range of from 0.0001μM to 100 μM.

Craine(US'941, hereafter) teaches a composition comprising tramadol and an opioid antagonist such as naltrexone(NTX), naloxoe or nalmefene. Especially, US'941

teaches that the effective amount of opioid antagonist is 1000-10,000,000 fold less than the amount of tramadol administered, see claims 6-7. For instance, table 16 utilizes the combinations of tramadol (50mg) and NTX(0.01mg, 0.1mg and 1mg, each).

As to the critical element required by the instant claims 362 and 373, Mole concentrations(i.e. 0.0001μM to 100 μM) are easily converted to grams measurement based on grams to mole conversion rule (i.e. grams of the substance/moles of the substance=molar mass of the substance in grams/one mole). For instance, 100 μM of NTX can be substituted with 34.14mg. Thus, the said limitation is embraced by the scope of the teaching of US'941.

Since both US'941 and instant claims are utilizing the very same opioid antagonists(e.g. naltrexone, naloxone or nalfemene) as an active agent, the recitations required by the claims 364-366(i.e. an inhibitor of ABC drug transporter or PGP drug transporter) are inherently met by the teaching of US'941.

Applicant is reminded that the claims are drawn to the composition where the claims are met when the structure of the composition is taught by prior art. In this case, naltrexone is inherently an opioid antagonist or an inhibitor of ABC drug transporters(or PGP or PGP1a), and thus, regardless how it is called by, the critical elements required by the instant claims are inherently met by the cited reference wherein the both patented and instant application utilizes naltrexone and the structure of the claimed composition comprising opioid antagonist(e.g.naltrexone) and non-opioid CNS active agent (i.e. tramadol) taught by the cited reference.

All the critical elements are well taught by the cited reference and the claimed subject matter is not patentably distinct over the prior art of the record.

5. Claims 362-365 and 368-376 are rejected under 35 U.S.C. 102(b) as being anticipated by Dante(US 5856332 or 5817665).

Dante(US'332 or US'665) teaches a composition comprising an opioid antagonist in combination with lithium and/or tricyclic antidepressant and/or a typical antidepressant, see claim 6(US'332) or claim 9(US665). Dante also teaches naltrexone as the effective specie of said opioid antagonist. The detailed teaching was mentioned in previous office action(see paper 8).

As to newly added limitations, Dante teaches that the preferable dosage regimen for naltrexone is about 10mg-150mg, see column 3(each patent). As mentioned earlier(rejection over Craine), the effective dose of opioid antagonist required by the instant claims in the range about from 0.0001μM to 100 μM(0.000034mg -34.14mg, respectively) is partially overlapped with the amount taught by Dante. Thus, the claimed amount is embraced by the scope of the patented inventions.

Naltrexone is inherently an opioid antagonist or an inhibitor of ABC drug transporters, and thus, regardless how it is called by, the critical elements required by the instant claims are inherently met by the cited reference wherein the both patented and instant application utilizes naltrexone and the structure of the claimed composition comprising an opioid antagonist(e.g.naltrexone) and a non-opioid CNS active agent (i.e. lithium) taught by the cited reference.

Response to Arguments

6. Applicant's arguments filed April 22, 2004 have been fully considered but they are not persuasive. First of all, the newly added limitations(i.e. 0.0001μM to 100 μM) is still embraced by the scope of the patented inventions(see above). Applicant's arguments with respect to lack of teaching about an inhibitor of ABC drug transporter proteins or an inhibitor of PGP(e.g. PGP1a) drug transporter which are required by the claims 364-366, the arguments have been carefully considered but are not persuasive because said limitations are inherently met by the cited reference because they are naturally an inhibitor of ABC drug transporter proteins or an inhibitor of PGP(e.g. PGP1a) drug transporter. For instance, tramadol is naturally non-opioid CNS active agent and naltrexone is naturally opioid antagonist regardless the latter terms are specifically used together to describe said compounds(e.g. tramadol or naltrexone). Thus, the composition comprising (a) tramadol or lithium; and (b) naltrexone, naloxone or nalmefene met the all the claims using different names(e.g. non-opioid CNS active agent, opioid antagonist, an inhibitor of ABC drug transporter, or PGP or PGP1a drug transporter inhibitor. All the claims are well taught by the cited references and the claimed subject matter is not patentably distinct over the prior art of the record.

Conclusion

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vickie Kim whose telephone number is 571-272-0579. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Chris Low be reached on 571-272-0953. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

VICKIE KIM
PRIMARY EXAMINER

Vickie Kim
July 15, 2004
Art unit 1614